

# **Exhibit 7**

**Summary:**

- Initial screen of CYP450 drug interaction potential of aegelin, *Aegle marmelos*, and OxyElite products was done using fluorescent based assay. This assay employs purified CYP enzyme and specific substrate. This is used as an initial screen to see if test compounds have any inhibition towards CYP450 enzymes.
- CYP3A4, 2D6, and 1A2 were tested, as these CYP isoforms are considered to play a major role in metabolism of more than 80% of drugs.

**Results:**

Test Compound	IC <sub>50</sub> (µg/mL)		
	CYP3A4	CYP2D6	CYP1A2
<b><i>Aegle marmelos</i> Friut Methanolic Extract</b>	<b>1.76 ± 0.36</b>	<b>NA</b>	<b>0.2 ± 0.08</b>
<b>OxyElite Pro (Super Thermo Powder)</b>	<b>69 ± 1.3</b>	<b>NA</b>	<b>NA</b>
<b>OxyElite Pro (Super Thermo)</b>	<b>89 ± 1.2</b>	<b>NA</b>	<b>NA</b>
<b>(+)-Aegeline (µM)</b>	<b>28 ± 1.75</b>	<b>NA</b>	<b>&gt;100</b>
<b>Ketoconazole (µM)</b>	<b>0.04 ± 0.01</b>	<b>NT</b>	<b>NT</b>
<b>Furafylline (µM)</b>	<b>NT</b>	<b>NT</b>	<b>2±0.1</b>
<b>Quinidine (µM)</b>	<b>NT</b>	<b>0.05 ± 0.02</b>	<b>NT</b>

NT= Not tested; NA= Not active

- *Aegle marmelos* fruit extract showed strong inhibition of CYP3A4 and 1A2.
- Aegleline and OxyElite products showed weak inhibition of CYP3A4 and no inhibition of CYP1A2.
- No inhibition of CYP2D6 with any test compounds

**CYP inhibition in human liver microsomes (HLM):**

- Based on these results, further testing against CYP3A4 and 1A2 in human liver microsomes was performed using widely used specific substrates (testosterone for CYP3A4, phenacetin for CYP1A2).
- For CYP3A4 inhibition, conversion of testosterone to 6 -hydroxytestosterone was quantified (HPLC) in presence of different concentrations of test compounds.
- For CYP1A2 inhibition, conversion of phenacetin to acetaminophen was quantified (UPLC) in presence of different concentrations of test compounds.

**Results:**

Test Compound	IC <sub>50</sub> (µg/mL)	
	CYP3A4	CYP1A2
<b><i>Aegle marmelos</i> Friut Methanolic Extract</b>	<b>10 ± 1.2</b>	<b>0.8 ± 0.02</b>
<b>OxyElite Pro (Super Thermo Powder)</b>	<b>NA</b>	<b>NA</b>
<b>OxyElite Pro (Super Thermo)</b>	<b>NA</b>	<b>NA</b>
<b>(+)-Aegelin (µM)</b>	<b>76 ± 2.8</b>	<b>NA</b>
<b>Ketoconazole (µM)</b>	<b>0.07 ± 0.01</b>	<b>NT</b>
<b>Furafylline (µM)</b>	<b>NT</b>	<b>2.6 ± 0.1</b>

NT= Not tested; NA= Not active

#### **CYP3A4 inhibition**

- *Aegle marmelos* fruit extract showed strong inhibition of CYP3A4 in human liver microsomes.
- However aegeline showed weak inhibition and OxyElite Pro extracts showed no inhibition of CYP3A4 in HLM.
- All the three extracts IC<sub>50</sub> values were significantly lower than fluorescent assay. These differences could be due the enzyme content in HLM and differences in the substrates used in the assay.
- The IC<sub>50</sub> values calculated from HLM are considered to be more physiologically relevant.

#### **CYP1A2 inhibition**

- *Aegle marmelos* fruit extract showed very strong inhibition of CYP1A2 in HLM. The IC<sub>50</sub> values were comparable in both assays. These results suggest that *Aegle marmelos* fruit have strong potential for causing drug interactions.